TWiV 1332 Clinical Update

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Guest: Daniel Griffin

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Vincent Racaniello: *This Week in Virology*, the podcast about viruses, the kind that make you sick.

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VR: From *Microbe TV,* this is *TWiV*. *This Week in Virology*, Episode 1332, recorded on June 18, 2026. I'm Vincent Racaniello, and you're listening to the podcast, all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: I see red on your bow tie. Today is Thursday, so nothing special there. What is it?

DG: Orange. It's orange.

VR: Orange.

DG: I have a yellow and an orange in this type of pathogen.

VR: Oh, so it's yellow fever.

DG: That's a good guess. It's actually

VR: I saw the yellow...

DG: It's prions. It's Creutzfeldt-Jakob's.

VR: Oh. How interesting. I just came back from Fort Collins, and at Colorado State, there's a big group of people who work on prions and chronic wasting disease. I think that was the first state where they diagnosed it years ago in deer.

DG: As our listeners may know, we were texting a little while you were out there. I spent about a decade in Fort Collins.

VR: It's a lovely city or town, I would say.

DG: It's very, very nice. I was fresh out of my training. I didn't know any better is really what happened. "I'll just go and set up a practice." I went out there, and I rented space and set up a practice. It was a great 10 years. Ten years later, my practice had grown to the largest internal medicine practice in town. I was chief of medicine at the academic center. Life was great. Then, for certain circumstances, we needed to move back to be close to my family. All my kids were born in Fort Collins.

VR: Wow. I liked it very much. Of course, it was beautiful weather. They tell me in the winter, it gets tough, right?

DG: It gets tough. I remember one time, it dropped five feet of snow in five hours. I'm at the office, and it starts snowing. I say, "Oh my gosh, we got to close up." We close up. Two hours later, there's two feet, three hours. Just imagine five, six feet of snow. It's over your head.

VR: My host, Tony Schountz, said there are underground passages in town. Because of that, in the old days, they couldn't get rid of the snow, so people had to go underground. Do you know about that?

DG: I didn't. That's kind of cool, right? That's like a mystery novel.

VR: I just found it very uplifting. The weather was great. There's no humidity there. The people are friendly. Maybe in five years, we'll move *MicrobeTV* there.

DG: Yes, see if I can buy my old house back. All right, let's jump in.

VR: Would you go back? You never know, right?

DG: You never know.

VR: You can't sail there, Daniel. That's the negative, right?

DG: That was actually a big thing. Our listeners probably know I love sailing. A big race coming up, actually tomorrow. Oh, my gosh. The Newport-to-Bermuda, 636-mile race. I would do this thing where I would work and do lots and lots of call. Then I would jump to the red eye, spend a week with my family here. Then I'd go back to work. Then I'd spend another week with my wife's family up in Cape Cod. I would somehow try to - but it's not the same as living here.

All right, quotation. Actually, speaking of sailing, Herman Melville, "Call me Ishmael," right? The author of *Moby-Dick*. This is an interesting one. This is, "We cannot live only for ourselves. A thousand fibers connect us with our fellow men." I thought that was very appropriate. As we read our first news piece, the Department of Health and Human Services has filed a motion to expedite its appeal of a court ruling that they say temporarily blocked changes to vaccine recommendations for U.S. children.

In a post on X, oh, my gosh, we've come to a world where people just post on social media. Robert F. Kennedy Jr. said, "The appeal seeks to restore the Advisory Committee on Immunization Practices so that the group, which has not met since last December, can issue vaccine recommendations ahead of the fall flu season."

VR: I don't know what you think about this, but I don't want this ACIP's recommendations because none of them know what they're talking about when it comes to vaccines.

DG: Well, that was the whole issue, right? I think it was Judge Murphy basically said it's supposed to be an expert panel. You need people on there who are experts. We don't just want your random minions, those sycophants who will do whatever you tell them to do. This is a group that should be populated with people who have expertise; they understand vaccines, they understand public health. It can't be just a bunch of people pushing a

nutraceutical anti-science agenda. They're appealing saying, "No, no, no, we're going to redefine what an expert is."

VR: No, you can't do that. We know what experts are.

DG: Yes, we really do. All right. Here's this next section. I'm going to put the glasses on because there's a lot here to read. "New plan scales back CDC's work on diseases abroad." We're already seeing that this has not been great so far. "The Trump administration is moving ahead with a plan that could decimate support for programs that detect and snuff out exactly such outbreaks. The new plan proposed by the State Department aims to overhaul the CDC's work on a landmark global HIV program that also helps countries manage surveillance for emerging diseases, strengthen lab networks, support childhood immunizations."

"The proposal is intended to diminish the agency's authority in the President's Emergency Plan for AIDS Relief." That's PEPFAR, right? It was created by President George W. Bush back in 2003. Probably saved 26 million lives. "Before 2025, USAID managed more than half of PEPFAR's budget. The CDC handled much of the rest. The changes may jeopardize the health of more than 12 million people on HIV treatment supported by CDC funds. The new plan would replace the health agency's budget for the work with a fee-for-service menu that requires countries to choose and pay for assistance from CDC."

"Any country that receives aid from the United States must pay for minimal administration support, and any country that receives more than $125 million in aid must buy a minimum package of some services, including population health surveys, the training program for disease detectives, and some disease surveillance, but not the integrated surveillance for emerging diseases. The new agreements do not set goals of eradicating polio or driving down HIV, tuberculosis pandemics, or maintaining goals in childhood mortality."

"It is anticipated they may skip support for polio eradication, vaccination during public health emergencies, and other items on the menu, as these countries have many other issues to spend money on." This is craziness. What is this?

VR: This is just obnoxious. It goes back to the Herman Melville quote, right? "A thousand fibers connect us." We have to help other countries. We always have. We don't have to charge for it. We have the money. The problem in this country is they just want to give it to certain people and not others. It's crazy, totally crazy. How can you charge people to be healthy in countries where they can't afford it?

DG: How do you charge people who don't have the money? This is like, "We have the ability here to help you prevent your population from dying, from being sick, but we're going to charge you, and we know you don't have the money."

VR: It's disgusting.

DG: It really is.

VR: It's just embarrassing as the United States that we're up. People need to realize, I think most Americans probably don't like this. There's a small fraction. Most Americans recognize that we have the ability. Very few countries can help other countries, and we are one of them, so we need to do this.

DG: Yes. At least the way I was raised, my religious upbringing was such that - this is not really in keeping with how I was taught.

VR: Oh, don't get into religion. My gosh. They're saying this is a Christian country now, this U.S. Well, religion means you care about other people, not charge them.

DG: Yes, that actually was what I was thinking about, this whole idea, "We're a Christian nation." I don't see this as being in line with the teachings of Christ, I just have to say. All right. I was going to say, let's be - anyway, the vaccine that prevents dementia. We actually have a couple of things here, and maybe we need a marketing spin. Anyway, this is actually, I thought, a very interesting article. The article, "Zoster Vaccination and Dementia: Interpreting the Signal and Testing Mechanisms," published in *CID*, it's a bit more speculation and lays out the potential mechanisms for why the shingles vaccine prevents dementia and the evidence we have.

I have to say, there's a lot of references here. We think this is what's going on. Actually, here's the evidence that we have so far. First, we have why the signal has gained credibility. We've actually shared a number of studies. I'm going to throw another one, actually, in today. We've covered this by referencing a number of same studies they reference and pointing out that this association has been replicated across a number of settings. Let's go through how. How is it that this might be happening?

They give us three ideas. One is reduced cumulative VZV reactivation burden, so that the chickenpox virus, the varicella zoster virus, can reactivate. You get infected when you're young, particularly in those that were not protected from vaccinations. Most of us in our age group, Vincent, and older, you get chickenpox, lays dormant, and then it can reactivate and does reactivate during your lifetime. Experimental systems add biological possibility to this idea that you just keep getting the chickenpox reactivation.

The VZV-infected brain vascular cells have been associated with amyloid beta, intracellular amyloid deposition, and amyloid and tauopathy-related transcription pathways. These findings support a possible link between the reactivation, vascular inflammation, and Alzheimer-relevant biology. I feel like we're going to return to that number three, which is kind of a recap. The other is immune remodeling beyond these specific effects. I think we've speculated this.

Maybe there's something about the vaccination that changes the immune function in older adults, including this baseline inflammatory activity and the magnitude or duration of responses to subsequent inflammatory stimuli. It may not even so much be the vaccine targeting, but it may be the adjuvant, the stimulation of the immune system. There are some small studies looking at the recombinant shingles vaccine and this AS01-adjuvanted vaccination, suggesting that it may actually have something to do with the adjuvant and the stimulation of the immune system.

VR: The effect is also seen with the original zoster-attenuated vaccine, right?

DG: Yes, it's better with the adjuvanted. We see it with both. I think that's a good comment. Then they basically say - I feel like this is circling back to one, that neurovascular intermediates of the reactivation. We do know that when you get reactivation, this can injure blood vessels, cause vascular injury, you can end up with strokes, you can end up with these microvascular brain injuries, and this could all accelerate cognitive decline or shift the

timing of the dementia diagnosis. In this framework, any association between the zoster vaccination and fewer dementia diagnosis could be made in part through this reduced vascular injury.

This is biologically possible, again, because, basically, we'll say shingles or varicella zoster vasculopathy is a recognized clinical entity. In some cases, the virus infects and inflames cerebral arteries, producing ischemic and hemorrhagic events and related vascular syndromes. There is, when someone has shingles, particularly if it's ophthalmic, you have this increase in stroke risk right around the time of the reactivation, looking into some of the mechanisms.

Here's another. If we don't have enough evidence that the Shingrix is now a dementia vaccine, and that's probably how we should market it. Who wants to reduce your risk of dementia? You want to get a shot to reduce that. The article “Dementia Risk After Recombinant Herpes Zoster Vaccination in Older Adults With a Recent Skilled-Nursing Facility Stay: A Target Trial Emulation,” published in *Annals of Internal Medicine*. Pretty robust study, cohort included over half a million, so 509,926 participants, median age 79. 8,843 received at least one of the recombinant zoster virus vaccine doses within 12 months after admission to the facility. Of these, 87% received it after discharge.

Receipt of the vaccine was associated with risk for dementia being 5.8 percentage points lower. Basically, they're seeing about a 24% reduction in your risk of getting dementia if you go ahead and get these shots. The interesting thing is some of the folks in here had had prior vaccination. For some of them, it was getting another dose.

VR: I think we ought to point out, though, that the biggest effect is in women. That's like a caveat.

DG: They even say here, associations were attenuated in men. Women are getting the biggest benefit here. Now, as I commented there, some of these folks are getting it again. They had it before. What about that? We have an article. Is that OK? Do you get a response? What happened? A lot of people ask, like, "Oh, I got my shot and my two shots when I was right around turn 50, turn 60, whatever it was. Should I get another? Can I get another? Is that OK?" We have the article, “Safety and Immunogenicity of 1 or 2 Additional Doses of the Adjuvanted Recombinant Zoster Vaccine Administered Five to Six Years After Primary Vaccination in Adults 50 or Older Years,” published in *Open Forum Infectious Diseases*.

Here, the participants were randomized to either one additional dose, two additional doses, or no additional doses. Then they're going to look at humoral and cell immunity, and they're going to evaluate them through a bunch of different ways. They're going to look at the anti-GE geometric mean concentrations. Geometric mean concentrations peaked about one month after one dose, and they give us numbers there. They declined at one year, but remained above pre-additional vaccine levels thereafter. They give us a different number for the concentration if you get this second dose. They look at the frequency of specific CD4 T-cells and memory B-cells. You find sort of a similar pattern.

You seem to be getting an additional boost, and is it safe? Well, pain and fatigue were the most common solicited adverse events. No serious adverse events. You do see a little bit of reactogenicity. Some folks have gotten this shot are familiar with this, but didn't look like there's any risk. I guess the next question is, does this make a difference?

Oh my gosh, screwworm, Vincent. We now have a screwworm dashboard. That's not good.

VR: Oh my, that's not good.

DG: I'll leave a link into this really nice USDA New World Screwworm dashboard. As of June 17, that's yesterday, right off the press, but actually it's up until 12th. They update it, but the date is from the 12th of June. We have 12 domestic cases so far, and you can see where they're clustered. They're mostly in Texas. There are a little bit active cases southeast New Mexico. They have this nice chart where you can see sheep, cattle, goats, dog, all the different-- We now have 12 confirmed cases in the U.S. Eleven of the 12 cases are in Texas. We've got that one right there in that New Mexico corner.

The first case was confirmed in a three-week-old calf on June 3. Most recent confirmed infestation of the parasitic fly, whose larvae feed on the living flesh of livestock and other animals, was detected on June 11 in a sheep in Sullivan County, Texas. Now, the CDC said that it's officially activated a Level 3 emergency response to support the USDA and the Texas Department of State Health Services in response to the NWS detections. Now, this is exciting, right, because that's serious stuff. Well, actually, Level 3 is the lowest of the CDC's emergency response levels. We're a little excited, but just not so excited, I guess, as this comes back in.

What to do? This is actually nice, hot off the press. FDA issues emergency use authorization for generic over-the-counter drug to treat new world screwworm in dogs and cats. I want you to think of this as a lot of us give our dogs and cats these types of medicines that protect them from the arthropods, right? The US Food and Drug Administration on the 11th issued an emergency use authorization for generic Nitenpyram for the treatment of new world screwworm infestations, the myiasis in dogs, puppies, cats, and kittens that weigh at least two pounds and are at least four weeks old. First generic animal drug authorized for use against New World screwworm.

They talk a little bit about how the flies lay their eggs in the open wounds or even mucus membranes of mammals, so it could be right inside the nose or the mouth, and then the larvae hatch, and they just burrow in, really, within hours. This is horrific. The whole idea is you give your animal a dose, and then you get a second dose six hours after the first. These are short-acting, so it's a treatment. It's not like you then don't have to worry. Different-sized tablets for different animals. I'll leave a link into the fact sheet for folks.

VR: Daniel, why are we having screwworm now in the U.S.?

DG: It's been going on for a while. We all want to blame everything on the current administration, but I think people had their guard down for a while. Back in the '60s, recognized huge problem. This was here in the U.S. We pushed it south using the irradiated males.

VR: Releasing irradiated males, right?

DG: Yes. You release the irradiated males. It's really interesting. Parasite Support has set out this update on it. It almost seems judgy, right? The lady flies, they only procreate once, and that's it for them, so if they have sex, we'll call it sex. You call it sex when flies do stuff? But anyway, flies have sex.

VR: Of course. Of course.

DG: When the flies have sex, the ladies only do it once, and that's then. It's with the sterile male, then that's the end of the cycle. Males are promiscuous: multiple times, multiple partners. That's why I felt it was judgy. These flies, oh my gosh, these irradiated males are just out there. One irradiated male can actually have sex with a whole bunch of ladies, and then they're all not going to have offspring. We did that, tens of millions of irradiated males. We released them, pushed it down to the Mexican border, pushed it all the way down, eventually to the Darién Gap.

VR: Darién Gap. Right.

DG: Then we were talking years ago about, "We're starting to see cases in Panama. This is a problem," and nobody - until now.

VR: Do we still release irradiated males in the U.S.?

DG: We can, but it's one of those things, right? You basically think of this as an irradiated male wall. It's a lot cheaper to maintain a wall that's, what is it, 100 miles versus thousands of miles, right? Try to cover the whole border with Mexico. That's what we need to do. We need to ramp that up because next thing you know, it's going to keep spreading north, so end up with Oklahoma. Colorado, it'll be in Fort Collins, infecting the animals there.

VR: I don't see why we're just not on this and getting - it's technically not hard to release irradiated flies. They've been doing it for a long time. Why aren't we doing it?

DG: It costs money. You'd have to take that money out of all those tax breaks for the rich, right?

VR: Oh, right. I forgot.

DG: You can see these people, they've already made plans on how to spend those tax breaks.

VR: It's just another -

DG: We're all in this together. You can't single out the rich people and take their money away.

VR: It's just another example of - this is old technology. We could be doing it. There's no need to have any cases of screwworm anywhere in the U.S., even Mexico, anywhere if it's so simple to do this.

DG: It is. This is the classic ounce of prevention worth a pound of cure. This is really expensive at this point to try to push this back down. We're sort of, "Oh yes, we're going to activate our lowest level." This is a huge problem, and this could turn into billions of dollars in losses for the cattle industry, which is not great, and also just the horror to the dogs, the sheep, the goats, the cats, the animals. I'm not so excited to go visit Texas and New Mexico while this kind of stuff is going on.

VR: Have there been any human cases in the U.S.?

DG: So far, none in the U.S., but over 100 down in Mexico. All right. Ebola.

VR Speaking of problems.

DG: Yes, speaking of problems. Predicting the future, right? I mean, this is going to be bad, and it already is bad. This is already in the top three. Is it going to be as bad as the West or the East African we'll talk about? We now have this nice WHO dashboard. We also have the CDC updates. They're pretty similar. Over 800 confirmed cases as per the WHO, as per the CDC. CDC has 196 confirmed deaths in the DRC. They say two. WHO says three in Uganda. Basically, about 200 confirmed deaths already. Let's talk a little bit about what we're hearing from different experts in the field.

Remember, this is the Bundibugyo. Remember when people used to have trouble saying that? Now we've said it so much, it's Bundibugyo, which is a type of Ebola virus species. Has only caused two previous outbreaks. There was a good discussion about this on the deep dive *TWiV* last Friday recording, Sunday drop. Both more than decade ago, and compared with other Ebola virus species, scientists have given it short shrift. I guess it was getting its feelings hurt. You can read the entire Bundibugyo literature in an afternoon, says Jens Kuhn.

VR: Jens.

DG: Jens. Jens Kuhn, a virologist who until recently worked at the Integrated Research Facility at Fort Detrick, a U.S. government lab. Do you know Jens?

VR: Of course. He's been on *TWiV* a couple of times. Yes.

DG: Been a bit of a star in his neglected area here. The lack of knowledge is worrisome, says Salim Abdul Karim, who runs the Center for the AIDS Program of Research in South Africa and chairs a panel advising the African Centers for Disease Control and Prevention on the Ebola outbreak. "This is the hazard, that we don't know enough about it," he says. As I mentioned, we're already looking at the third-largest Ebola outbreak to date, and we hear that Ebola outbreak in DR Congo expands into a large displacement camp. That's the new terminology, basically like a refugee. These are displaced people who have nowhere else to go.

This is a bit of a disaster, right? This is a camp with 30,000 displaced people living in cramped and unsanitary conditions. Two victims were living in this Kampagba Camp. Once you end up with an Ebola viral outbreak in this kind of a setting, it's a disaster. This camp has actually had some issues. There's been conflicts with the government and rebel groups. Just to put a human face on it, it was a mother and a daughter who died on May 31 and June 1, and later tested positive for Ebola. That's a big thing we've been talking a little about, this issue with not having accurate tests.

This outbreak's been going on for months now. I think we all know now this. The problem was, early on, people even thought, "Hey, maybe this is Ebola," and they sent off tests, but the tests didn't pick up the Bundibugyo. They came back negative. "It's not Ebola. It's probably Lassa. Maybe it's malaria. You'll be just -" whatever.

VR: "Go home. Just go home. You'll be fine."

DG: Yes. Not only do you lose those people, not only do they spread it to all their contacts,

not only spread to everyone at the funerals when you go through that process, but the healthcare workers die because they get exposed. They die, and they don't know what's going on. Then how do you take care of people if you don't have the staff and the trained personnel?

VR: This refugee camp or displacement camp is a real problem because there's no way you can do infection control there. 30,000 people, I'm sure they're cramped and unsanitary. This could be a real problem.

DG: Yes, that's what we're predicting. Congo Ebola outbreak may be worst ever, Africa CDC says. The head of Africa's Centers for Disease Control and Prevention warned that the Ebola outbreak in Congo could be the worst ever, saying that, "Currently, tens of thousands of contacts of those ill with the disease have not been traced. If we don't stop this outbreak very soon, it will be worse than we had in West Africa and Eastern DRC." This is from Africa's CDC Director, General Jean Kaseya. He's referring to that outbreak. I think a lot of people know about the Guinea, Liberia, and Sierra Leone 2014, 2016, that killed over 11,000. The other was the 2018 outbreak, also in the Congo.

The other is a little bit interesting. I don't know if you read this full letter. We're trying to do trials, theoretically, to find out what actually really works. As mentioned, you could read the entire literature in an afternoon on Bundibugyo. There's some small molecules, say antiviral, but there's also a monoclonal antibody that some evidence might be helpful. All of the stash of this particular monoclonal antibody, it's a cocktail from a survivor, this MBP134.

There's this request or this letter to the government basically saying, "Would you release that for a trial to see if it really works?" They're holding onto it saying, "Oh, if Americans get it, we want to have this." One, we don't really know if it works. Let's find out if it really works, and if it does, then potentially you could ramp up production. Right now it's just sitting there.

All right, hantavirus. Vincent, the sky is falling, isn't it? What is going on in this world? This I like. It's one of those things like we have such a short attention span, and we can't have such a short attention span because people are finally, I think, properly asking this question. We've got the article, “How Did the Cruise Ship Hantavirus Outbreak Start? Scientists Are Investigating New Scenarios.” This was published in *Science* - I thought this was really well-read. It's written by Kai Kupferschmidt. I'm just going to read a little bit of it, and then you and I can chat.

"When news broke of a deadly outbreak of a rodent-borne hantavirus aboard the cruise ship MV Hondius last month, it took only hours for wild conspiracy theories to start to circulate about how it might have started. Was this a side effect of COVID-19 vaccines? Did the virus leak from a lab in Australia this time? A more prosaic and plausible origin story also took hold quickly. The first patient, a 70-year-old Dutch man who died aboard the ship on 11 April, could have come in contact with rodents carrying hantavirus while he and his wife were birdwatching at a landfill in this city on Argentina's southern tip, where the cruise ship started on the 1first of April." Now, his wife died two weeks later on her way back to the Netherlands.

Here we go. "Even that story never made much sense," as Gustavo Palacios, a virologist at the ICON School of Medicine in Mount Sinai, "No hantaviruses have ever been reported around this city, and the region has never seen cases of the disease they cause, hantavirus

pulmonary syndrome. Palacios and a large group of other researchers are now investigating several other possible scenarios, including some that would revise scientists' knowledge of where the virus circulates or its incubation period."

"Although researchers were skeptical of the link to Ushuaia, that's a city from the start, it has only become more unlikely as they gathered evidence. The Dutch passengers arrived in Ushuaia on 29 March, and the man is now understood to have developed a fever just five days later, on the third of April. Too short an incubation period." "Such a short incubation period is not impossible, but it seems very unlikely," says Valeria Martinez, a virologist at Argentina's National Institute of Infectious Disease and a collaborator on investigation."

VR: I think that's very interesting. Also, the rice rat, I forgot the full name, the reservoir of Andes, is not found in this landfill in Ushuaia, so they probably got it somewhere else. The idea is maybe they were far north, and a mouse got into their camper.

DG: You obviously read this article. They were living in this camper thing for a while before they got on the ship, before they went to this place. It's starting to be more plausible that - one incubation period. That's important to know. The idea that he got sick five days after, this would be the shortest incubation in history, which - OK, so maybe -

VR: The other thing is that the genome sequences now line up with isolates far north.

DG: Hundreds of miles, yes, so not -

VR: Where they were, but they were there in February. They couldn't have gotten infected in February because it's too long an incubation period. Then they did examine the camper and didn't find any mouse poop in it, so this is still ongoing, obviously.

DG: It's a good article because it goes into all the stuff.

VR: It's very good. It's excellent.

DG: Excellent article. We'll keep an eye as we hopefully figure out where it's from. All right, measles. We are up to 2,163 cases so far this year in the U.S., as per the - that's the Johns Hopkins tracker, over 2,000. The CDC says 2,073, but we're over 2,000. Just to give you what are we headed towards, 2,242 is what we ended up last year, so we're on our way. We're adding about 30 cases a week at this point, so is that at one, two, three - we'll be there by the fall.

Canada, increasing up there as well, but only eight new measles cases, so they're over 1,000 already up in Canada, but Virginia, where my daughter, Eloise, has just started as an elementary school teacher, is the new nation's hotspot. Be careful, Eloise. Don't breathe.

VR: Well, I'm sure she's vaccinated, right?

DG: She is. She is, yes.

VR: Hopefully, the kids are too.

DG: Well, I think that's the issue. It is interesting, right? My daughter, she's teaching summer school at one of these, they call it a title something. It's an area where there's less resources, economically challenged, et cetera. A lot of these same areas, you end up with

lower vaccination rates and less education, et cetera, but then I'm thinking like, "Oh, she's elementary, these are these young kids." Virginia, we're up to 121 cases.

What's really interesting, and most of them are just happening now, this is ongoing, is a third of them are in the 18 and older. It's sort of an interesting shift. Most of what we've seen is sort of the under 12, right? Here we're seeing a quarter of them are 0 to 4, a third are 5 to 12, 15% are that 13 to 17, and then 30% are 18 or older, so we're starting to see an older shift.

All right. Let's move on to flu. We're going to talk about, “Influenza Vaccine and Associated Infection and Death in California, 2024 to 2025,” published in *JAMA Network Open*. This is a case-control study of linked diagnostic test results, immunization records for over a million California residents. Influenza vaccination. This is interesting because we always say that vaccines don't prevent infection, they prevent illness. Here we're actually seeing 40% lower likelihood of lab-confirmed influenza. In the short term, they do also reduce your risk of infection.

Among adults aged 65 years and older, we were only seeing about a 30% lower likelihood of death due to influenza-related causes. We got both here: 40% lower risk of ending up with the flu, 30% lower risk of dying from the flu. They have a really nice figure where you can see really getting the most benefits. With the FluMist, the stuff up the nose in the 2 to 17-year-olds, that was like a 60% reduction.

VR: My feelings are that this is good because 40% is better than nothing, but it could be better, right?

DG: I think it could be better, yes.

VR: People are working on improving the flu vaccines. I don't know what you need to do, but still, people should not be discouraged by - 29% lower likelihood of death is pretty good.

DG: Yes. Also, as we'll see with vaccines, it isn't just your likelihood of not dying from flu, but a lot of times you get the flu, you get COVID, you end up having a heart attack or a stroke. Let's move on to COVID because we have a study right in that line, but let's look at our multicolored lines. As I put this in, I was thinking, my kids use this term rage-baiting. Are you familiar with rage-baiting, Vincent?

VR: No.

DG: You say something that gets someone all full of rage, and that's really - you see it among siblings. They rage-bait each other. I don't know if we called it that. We certainly did a lot of that when I was a young brother. We look at multicolored lines, and look at this. COVID, it's going away. We're never going to see it again, Vincent.

VR: Well, I don't know about that, Daniel. I think we will. It's just a question of whether we're going to see this summer surge in July, which is coming up. Two weeks, we should start seeing, but it's really flat still. No question.

DG: No, it's going away. We are never going to see COVID again. I'm just following the line out. Put my ruler there.

VR: Have you seen any cases this summer?

DG: I haven't seen in weeks. I've not seen a COVID case in weeks. This is great stuff. Here, as we were just talking about, seasonal, this is a correspondence that was published in *The Lancet Infectious Diseases*, "Seasonal Influenza Versus COVID-19 Hospitalization Risk During the 2025-2026 Influenza Season." Here, they're using U.S. Department of Veteran Affairs electronic health records, and they compared the risk of hospitalization among individuals with multiplex-based lab-confirmed seasonal influenza versus COVID-19 during this season.

Compared with COVID-19, seasonal influenza was associated with a higher risk of hospitalization, 1.43, corresponding to a risk difference of about 48 hospitalizations per 1,000 people. Kind of interesting.

VR: I wouldn't have predicted that.

DG: It was a bad flu season.

VR: That's a good point. It could change from year to year.

DG: I think that's important to realize. I have a nice breakdown. You can see all the different breakdown individuals: hypertension, elevated cholesterol, chronic lung disease, cardiovascular, breakdown by race and age.

VR: This is not a contest. You should still get immunized against both, right?

DG: I think that's funny. It's not a contest. It's not a competition. All right. Now, this is a little pet peeve of mine as we keep putting on the yellow gowns and the gloves and everything when we go in that COVID room. The article, "Discontinuing Contact Precautions for COVID-19: The Science Says It's Time," was published in the journal *Infection Control & Hospital Epidemiology*. This is open access, so read away.

We read here that, "The CDC has recommended contact precautions for healthcare personnel in caring for COVID-19 patients since the beginning of the pandemic. Then I'll just add, and they've never changed. "However, current scientific evidence points to transmission through small respiratory droplets or aerosols, infectious respiratory particles, and not contaminated fomites as the dominant routes of transmission of SARS-CoV-2. We believe science shows there is no benefit and thus only negative consequences to patients, the environment, and the U.S. healthcare system associated with ongoing contact precautions for patients with SARS-CoV-2 infection. We advocate for updated guidelines reflecting current science."

VR: You support this, Daniel?

DG: I do. I support this message.

VR: You have talked about this before, right?

DG: Yes. We go into the room with a patient with COVID, right? We put the mask on, put the respirator on, the N95. That makes sense because it's these infectious respiratory particles. Then we put on these $8 per yellow gowns, or they get some blue ones. We put gloves on. It's this whole thing. If anything, it reduces the people going in the room because it's like a whole donning and doffing. Really, it's not a contact issue. It's a respiratory.

VR: You probably should wear gloves anyway in general when taking care of a patient?

DG: Either we wear gloves or, between patients, before and after, you lather up with the alcohol, or you're going to do soap and water. You've really got to wash your hands multiple times. If you don't have a buzz by noon from all that alcohol that you've been washing your hands with, you're not washing them enough. I joke about it. It's funny. There was that article. It's quite a while now where they - false elevation of blood alcohol level from hand alcohol. I was like, "It's not false. It's a low level." You keep putting that stuff on your hands, particularly like ER docs with a lot of patient volume.

VR: I guess it's absorbed through the skin, right?

DG: Yes.

VR: Interesting.

DG: All right. The article, "2024, 2025 COVID-19 Vaccine and Major Adverse Cardiovascular Events among U.S. Veterans," published in *JAMA Internal Medicine*. Maybe we start asking people, "Hey, do you want to get your yearly heart attack prevention, stroke prevention vaccine?" because we don't. When you get into the winter respiratory season, you get the flu, you get COVID, we see an increase. We know from other studies, and we're going to see it again right here, that vaccination reduces your risk of a stroke or heart attack during the winter season. This cohort study included over a million participants. Sounds familiar again from the U.S. Department of Veterans Affairs, right?

They found that the 2024, 2025 COVID-19 vaccination was associated with a lower risk of COVID-19-associated major adverse cardiovascular events. More prominent reductions among those 75 years or older, those with comorbidities. Secondary analysis of all-cause major adverse cardiovascular events showed substantially large absolute risk reductions. They used the VA electronic health record database. We talked about that just earlier. Over a million participants, and they break them down.

At eight months, the COVID-19 vaccine was associated with a lower risk of COVID-19-associated major adverse cardiovascular events. Vaccine effectiveness, VE, so we don't know effectiveness or efficacy, 37.7%. Almost a 40% reduction ending up with a heart attack or stroke.

VR: For elderly people, this is a no-brainer, especially since the vaccine does not have adverse events associated with it, particularly in that age group, right?

DG: No, it's very well-tolerated. If you add a little bit of reactogenicity with the mRNA stuff, and you don't like that, we also have the Nuvaxovid.

VR: Nuvaxovid.

DG: Nuvaxovid. How do you pronounce it?

VR: Nuvaxovid.

DG: Nuvaxovid.

VR: Yes, just very simple.

DG: Like new, the Nuvaxovid.

VR: Yes, new vaxovid.

DG: The new one. Nuvaxovid. I don't want that mRNA. I want that Nuvaxovid.

VR: It's new vaccine for COVID. Nuvaxovid, right? Makes perfect sense.

DG: The Nuvaxovid. Oh, I like this. OK. Still, they need to work on the naming. All right. Well, I will wrap this up really the way we started with no one is safe until everyone is safe. We're all connected by that thread. Right now, and it turns out very appropriate, we're doing our May to July Foundation International Medical Relief of Children fundraiser. They're right there in eastern Uganda, right in the thick of this with the Uganda outbreak, with the Ebola outbreak. We are going to double your donations. We're hoping to send them a maximum donation of $10,000. A lot of people have already stepped up, so thank you.

This is a great way to make a difference. Not a lot of waste here. This is really going to efforts on the ground. Go to parasites.borders.com, click the Donate button, and we will continue to support FIMRC.

VR: We complain a lot about U.S. cuts to foreign health aid. This is one way that you can counter that by donating, right? This is directly going there, independent of the U.S. government.

DG: Yes.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Susan writes, "Thank you so much for your *TWiV* podcasts. I've been an avid listener since the beginning. As a kidney transplant recipient, I'd like to have you call attention to the fact that Xocova may not be appropriate for those taking any form of tacrolimus. My understanding is that Xocova can create very high concentrations of tacrolimus, just as Paxlovid can. Luckily, other family members can help protect others."

DG: Susan, this is a great thing. Actually, it's really good you point this out because I've been on panel discussions with other physicians. The Paxlovid folks have done a really good job of, I think, letting people know, "Hey, P450, drug interactions, be careful. It can raise the tacrolimus levels. This could be a problem." Tacrolimus is one of the medicines that folks use when they've got a kidney transplant, for instance. Ensitrelvir, Xocova, same deal, same issue, same mechanism, but a lot of people don't think about it.

As Xocova starts to get used, we've got to keep giving people the heads-up that it's the same interaction. The same medicines can have impacted levels, whether there's statins, or tacrolimus, or some of the other medicines metabolized through the P4 cytochrome, P450 pathway, CYP3A.

VR: Terri writes, "Decades ago, I heard a theory that having the initial herpes zoster infection may lead to some people developing type 1 diabetes. I believe the thought was that the sensitized immune system might mistakenly attack the insulin production area. I don't find anything with a simple internet search. Has Daniel ever heard about this, that it proved to be false, and has the rate of type 1 diabetes fallen during the years we have had an effective vaccination for herpes zoster?"

DG: I don't know about this, but I like this. This is actually one of those things you can

investigate, in basically, a dry investigation. You can start asking, looking at rates of type 1 diabetes, looking at areas relative to vaccination rates, is that impacting? I don't know about this, but definitely Terri from Boulder, Colorado.

VR: Another Colorado, yes.

DG: This is an interesting question.

VR: Brian writes, "Thank you for your tireless efforts, brave candor, scientific expertise, and timely clinical updates. I felt compelled to send an email after hearing that one of Daniel's daughters graduated from William and Mary and will be teaching fourth grade at Magruder Elementary. I'm a family physician now, but my father was an administrator at William and Mary, and I was once a fourth-grade student myself at Magruder Elementary School in Williamsburg, circa 1985. My fourth-grade teacher, Mrs. Linda Bowe, was one of the best I ever had. Like many great teachers, she helped shape the world through diligent, caring, inspirational, and quietly powerful ways."

"Godspeed to your daughter as she begins her teaching career, a calling as impactful as what we do in science and medicine, for sure. By way of questions, I have more of a request for educated speculation. As a primary care doc, I am interested in both the short and long game. In terms of COVID treatment with antivirals, reducing hospitalization and death are great short games, but I've always had an interest in knocking down viral loads early, hoping to reduce the cumulative burden of each infection upon long-term cardiovascular health, neurological sequelae like Parkinson's and dementia, and wear and tear manifest by brain fog, decreased exercise tolerance, and even mental health deterioration that I've seen in many of my patients after COVID."

"In the absence of trials spanning five, 10, 20 years out, do you think it's intuitively acceptable to offer antivirals to any patient with COVID regardless of their having high-risk factors, Paxlovid for proven symptom reduction, but also for potential long-gain benefits that may never be proven in adequate RCTs? Thank you."

DG: This is a great email. I'll have to let my daughter Eloise listen to this. I like the nice connection with Magruder Elementary. This makes sense, right? We've talked a lot about the mechanism of why these things are happening. I think this is where, when a medicine first comes out, we study it in a particular population. You want to study it in a high-risk population so you can see that benefit. Over time, we don't just restrict therapy to the targeted studied population. We extrapolate. Why would you let an infection go unchecked, particularly with all we understand? I think a lot of what you're thinking here, writing here makes sense.

VR: Ryan puts links to the obituary of Mrs. Linda Bowe. Also, he wrote a post on Substack about this idea with Paxlovid. You have to read it, Daniel, because you get a shout-out.

DG: I'll do that.

VR: Valentina writes, "Love, listening to you on *TWiV*. I'm flying to Argentina with my one-year-old son in a couple of weeks. It's flu season there as it's in the southern hemisphere, but unfortunately, I can't find a flu vaccine in the U.S. since they have not received them yet. I also called my son's pediatrician and travel clinics, but no luck. Any advice? I brought a flu/COVID RSV test to take with me, but that's about all I can think to do."

DG: I would probably reach out to some of the local big chain pharmacies and see if they have any sort of it. That's that weird zone you find yourself in where they've run out of the seasonal from before. They haven't gotten the new ones. They won't get them until August, September. Probably the best you could do is reach out to some of the pharmacies, see if anyone's got some.

VR: Joe writes, "My wife and I love *TWiV*. We've been listening for several years now. We are both retired from NIAID. She was a research nurse, and I was a program officer. We now live in South Carolina in a retirement community. Last week, we were told that one of the residents of our community had come down with a case of measles. The South Carolina Department of Health was doing contact tracing and contacted my wife to tell her that she had come in contact with this person at the local gym. They told her to quarantine for 21 days, but if she got laboratory proof of immunity with a measles antibody titer, she didn't have to quarantine."

"She did get the titer done, and it seems she has a high enough titer to be considered immune. The test report said a titer above 16.49 was consistent with immunity. Her result was over 300. The test also gives results for mumps and rubella. Her mumps was 27.6 and her rubella titer 14.8, both above the limit for immunity, 10.99 and 1, respectively, according to the report. I was wondering whether her relatively high titer for measles might indicate that she actually had come in contact with the virus recently and effectively got a recent boost from it. Do you think it's possible? She was born in 1957, but can't remember if she got the vaccine or had a case of measles."

DG: I like that speculation. That was the first thing that came to my mind when I see greater than 300, is like, "Wow, was she exposed and got a boost at some point?" I wouldn't know how recently. It probably was not this one that just happened because it takes a little bit of time, but I don't know. We're starting to see measles again. There may have, at some point, been, whatever, either the initial vaccine or infection, and then probably another exposure gets you that boost.

VR: It's a very high titer.

DG: Off the chart.

VR: Unlikely that you've maintained that since the '50s, right?

DG: That would be my thought, yes.

VR: That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

DG: Oh, thank you. Everyone, be safe.

[music]

[00:54:44] [END OF AUDIO]